How is Knowing the Human Genome Good for Medicine?

by Jeffrey H. Simonson

The Human Genome Project is producing data about our genes at an ever dizzying rate. At the end of this project will have complete genetic and physical maps of a human genome. We will also have complete sequences of not just our ~75,000 genes, but every one of our ~3,300 million bases. Additionally, we will have information on genetic mutations conferring heritable and sporadic diseases. This is an incredibly large amount of data. To store the entire human DNA sequence on a computer would take a disk with the capacity of 8.25GB (8.25×10^9 bytes or 66×10^9 bits). This is equivalent to ~2 million pages of printed text taking up maybe 10,000 books. Only in 1997 did magnetic and optical storage disks reach this capacity. Though this enormous dataset will undoubtedly be useful in genetic research for many decades, how practical will it be to the majority of people helping pay for it? In particular, how can knowledge of the human genome help improve life-enhancing technologies such as medical care? Three of the most significant ways are:**1)** presymtomatic screening for diseases; **2)** genotype-specific disease therapy; and**3)** disease risk assessment based on geographic variation of alleles.

PRESYMTOMATIC SCREENING: Detection of diseases before symptoms are visible allows treatment before too much damage is done or the affliction is untreatable. This can be done using the Polymerase Chain Reaction (PCR) to amplify a known disease locus. Allele-specific PCR, or sequencing of PCR products, can determine which alleles an individual has and therefore the individual's risk of contracting a disease. PCR, however, requires oligonucleotides complementary to each end of a locus. The knowledge of which loci to amplify and the exact sequence of potential priming sites will come from human genome databases. This technique is particularly useful in screening infants for retinoblastoma where conventional detection requires anaethesia and the disease is curable with early detection. Early detection of disease-causing microorganisms is also possible using PCR. Information from human and microorganism genome databases could be used to design PCR primers able to amplify microorganism sequences but not human sequences. Detecting diseases with long latency times, such as Hepatitis B and Lyme disease are good candidates for this approach. PCR can also be used to detect minimal residue of diseases such as leukemia where some disease cells may still exist after chemotherapy.

*GENOTYPE-SPECIFIC THERAPY:*Presently, all individuals presenting symptoms of a particular disease are treated in the same way. For example, hypertension is normally treated with a low-slat diet, but some patients respond poorly to this treatment. For diseases with complex mechanisms, not all individuals will have the same defect causing the symptoms. These differences are likely caused by different alleles, or mutations in different genes. Knowing which treatments are most effective for each particular allele and an individual's genotype would increase effectiveness of treatments. Much of this information will come from genomic databases. One problem in this approach is the distribution of drugs toxic to some portion of the population.

GEOGRAPHIC RISK ASSESSMENT: As information about population-level human genetics grows, so will its use. Knowing the allele frequencies of distinct populations for disease-causing loci will be useful for risk assessment in individuals from a given population. If we know the risk of disease for each allele, then we can predict the risk of an individual contracting a disease even without family history. Our family histories still exist in our genes. This information can also give us levels of penetrance for some diseases. Therefore, knowing an individual's genotype, allele frequencies of closest relatives (ethnic origin), and a disease's penetrance, can help us determine the chance a particular disease will occur. We can also decide if certain populations need to be genotyped. If the genetic component of a disease is very low (as opposed to the environmental component), then the population does not need genotyping. This is similar to the case of breast cancer. Since only 5-10% of breast cancers appear caused by germline mutations, then there is no need to test individuals for mutations in BRCA1 or BRCA2 unless they have some other predisposition.

Building gigantic databases containing detailed knowledge of human genomes is expensive and time consuming. The benefits of this work may not be realized for many years. Still, it is a worthwhile endeavor if only for its use in human medicine.